UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,944	06/21/2006	Kevin A. Gray	564462003900	2689

45975 7590 06/22/2009

VERENIUM C/O MOFO S.D.
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
06/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,944	GRAY ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,46,56-58,61 and 133* is/are rejected.

7)☒ Claim(s) *133 and 275* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,46,56-58,61,73,125,126,130,131,133,135,137,138,140,169,171,218,221,225,229,231-234,236,241 and 271-275.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 73,125,126,130,131,135,137,138,140,169,171,218,221,225,229,231-234,236,241 and 271-273.

Application Status

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/21/09 has been entered.

In response to the Final Office Action dated 01/21/2009, applicants filed an RCE received on 04/21/09 is acknowledged. In said response, applicants' amended claims 1, 46, 61, 73, 125, 130, 131, 133, 135, 137, 140, 169, 171, 218, 221, 225, 229, 231-234, 236, 241 and 271-274, and added a new claim 275.

Furthermore, in the light of the instant amendment, applicants have argued that "unity of invention exists between the restricted groups (Groups II to XXII) with the elected Group I, as all the claims are closely related and also possess novel inventive concept and can be properly added back to elected Group I. Applicants' request has been considered, however, the instant amendments to the claims in elected Group I is not in a condition for allowance and the claims in the restricted groups (Groups II to XXII) as written are also not in a condition for allowance as said claims do not meet the enablement and written description requirements (see rejections below).

Hence, for the above cited reasons searching of all claims is a serious search burden and contrary to applicant's argument, the requirement is still deemed proper and is therefore made FINAL.

Claims 1, 46, 56-58, 61, 64, 66, 68, 70, 73, 125, 126, 130, 131, 133, 135, 137, 138, 140, 157, 161, 169, 171, 218, 221, 225, 229, 231-234, 236, 241 and 271-275 are pending in this application, claims 73, 125, 126, 130, 131, 135, 137, 138, 140, 169, 171, 218, 221, 225, 229, 231-234, 236, 241 and 271-274 remain withdrawn as they are drawn to non-elected inventions. Thus, claims 1, 46, 56-58, 61, 133 in part and added new claim 275 are now under consideration.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Withdrawn-Claim Rejections 35 USC § 102

Previous rejection of claims 1, 46, 56-58 and 61 in part rejected under 35 U.S.C. 102(b) as being anticipated by Bult et al., (Science, 1996, Vol. 273 (5278): 1058-1073), is being withdrawn due to amendments to claims.

Withdrawn -Claim Rejections 35 USC § 103

Previous rejection of claims 1, 46, 56-58 and 61 in part rejected under 35 U.S.C. 103(a) as being unpatentable over Bult et al., (Science, 1996, Vol. 273 (5278): 1058-1073), is being withdrawn due to amendments to claims.

Maintained-Claim Objections

Claim 133 contains non-elected subject matter such as immobilized polypeptide (depending from non-elected claim 73), the heterodimer (depending from non-elected claim 126), the antibody (depending from non-elected claim135). Appropriate correction is required.

Applicants' have traversed the above objection with the arguments "that after the elected product claims (Group I, including claim 133) are found allowable, the withdrawn

process claims (Groups II-XXII), that depend from or otherwise require all the limitations of an allowable product claim should be rejoined" (page 16 of applicants' response dated 04/21/09).

As argued by the examiner above, the instant amendments to claims do not rectify the objections and therefore the objection is maintained.

New-Claim Objections

Claim 275 recites the phrase "…the complement of a nucleic acid sequence…", it is not clear to the examiner whether the complementary polynucleotide claimed is full length or partial complement of the claimed sequence, examiner suggests amending the claims to recite "…the full-length complement of a nucleic acid sequence…".

Maintained-Claim Rejections: 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for an isolated polynucleotide of SEQ ID NO: 7 encoding the polypeptide of SEQ ID NO: 8 having glucoamylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions to the full-length complement of SEQ D NO: 7 and encodes a polypeptide with glucoamylase activity, isolated host cells comprising the polynucleotide (as in claim 61) and a micro-array comprising said polynucleotide (as in claim 133), does not reasonably provide enablement for any isolated polynucleotide having at least 95% nucleic acid sequence identity with polynucleotide sequence of SEQ ID NO: 7 encoding a

polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions (as in claims 1 and 46), vector comprising said polynucleotide (as in claims 56-58), isolated host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

The breadth of the claim: Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function or guidance

regarding variants/mutants or fragments of polypeptide of SEQ ID NO: 8 having several distinct activities.

Claims 1, 46, 56-58, 61 and 133 are so broad as to encompass any isolated polynucleotide having at least 95% nucleic acid sequence identity with polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions (as in claims 1 and 46), vector comprising said polynucleotide (as in claims 56-58), isolated host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to extremely large number of polynucleotides and encoded polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function.

However, in this case the disclosure is limited to an isolated polynucleotide of SEQ ID NO: 7 encoding the polypeptide of SEQ ID NO: 8 having glucoamylase activity, or a polynucleotide sequence that hybridizes under defined stringent conditions to the

full-length complement of SEQ D NO: 7 and encodes a polypeptide with glucoamylase activity, isolated host cells comprising the polynucleotide (as in claim 61) and a micro-array comprising said polynucleotide (as in claim 133). It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and encoding polypeptides that are having at least 95% nucleic acid sequence identity with the nucleic acid sequence of SEQ ID NO: 7 and encoding a polypeptide having glucoamylase activity or a polynucleotide encoding enzymatically active fragment thereof of SEQ ID NO: 8 wherein the fragments have glucoamylase activity. The specification is limited to teaching the use of a polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a polynucleotide encoding an amino acid sequence of SEQ ID NO: 8, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make and use the claimed polynucleotides and encoded polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (for example, see Whisstock et al., Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003, Aug. 36 (3): 307-340. Review), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple

modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any isolated polynucleotide having at least 95% nucleic acid sequence identity with polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions (as in claims 1 and 46), vector comprising said polynucleotide (as in claims 56-58), isolated host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133), because the specification does not establish: (A) a rational and predictable scheme for modifying specific nucleotides in the polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions; (B) regions of the protein/polynucleotide structure which may be modified without affecting the desired biological activity of the encoded polypeptide; (C) the general tolerance of the polypeptide and the encoding polynucleotide to modification and extent of such tolerance; (D) a rational and

predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological activity; (E) the tertiary structure of the molecule and folding patterns that are essential for the desired biological activity and tolerance to modifications; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides and polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1975)). Without sufficient guidance, determination of polynucleotides and polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants' have traversed this rejection with the reasoning, "…the scope of the claims has been amended so that nucleic acids of claim 1 encode polypeptides having glucoamyalse activity and no longer include nucleic acids encoding polypeptides having all of the catalytic features (several distinct features)…" (page 16 of applicants' response dated 04/21/09).

Reply: Applicants' arguments have been considered and found to be non-persuasive as pointed out in the above rejection and supported by scientific reasoning, see provided explanation below.

While methods to produce variants of a known sequence, such as site-specific mutagenesis, random mutagenesis, etc., are well known to the skilled artisan, producing variants capable of having glucoamylase activity, requires that one of ordinary skill in the art know or be provided with guidance for the selection of which, of the infinite number of variants, have the activity. Without such guidance, one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. For the rejected claims, this would clearly constitute **undue** experimentation. Guo et al., (PNAS, 2004, Vol. 101 (25): 9205-9210) teach that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a model, is 34% and that this number is consistent with other studies in other proteins (p 9206, paragraph 4). Guo et al., (*supra*) further show that the percentage of active mutants for multiple mutations appears to be exponentially related to this by the simple formula $(.66)^{x}$ X 100% where **x** is the number of mutations introduced (Table 1). Applying this estimate to the protein recited in the instant application, 95% sequence identity allows up to 93 mutations within the 1866 nucleotides of SEQ ID NO: 7. For argument sake, even if one assumes only 1/3 of the 93 nucleotide mutants/changes result in amino acid changes that result in mutations that do not affect the glucoamylase activity of the encoded polypeptide, the number of likely changes will be still around 62 nucleotide changes that results in amino acid

changes that affects the glucoamylase activity and, thus, only $(0.66)^{\wedge 62}$X 100% equivalent to **$6.4x\ 10^{-10}$%** of random mutants having 95% sequence identity to encoding polynucleotide of SEQ ID NO: 7 would be active. Current techniques in the art (i.e., high throughput mutagenesis and screening techniques) would potentially allow for finding a reasonable number of active mutants within about a hundred thousand inactive mutants. But finding a few mutants within several trillions or more, as in the claim to 95% sequence identity to encoding polynucleotide of SEQ ID NO: 7 would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Applying this estimate to the instant protein, a functional equivalent thereof with 95% sequence identity to encoding polynucleotide of SEQ ID NO: 7, as recited in claims 1 and 46 (in fact, claim 46 is even broader in scope), an extremely low number of active mutants will be present among an enormously large number of inactive mutants and as such screening for these active mutants would be burdensome and undue experimentation when there is no guidance provided in the specification.

Maintained-Written Description

Claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 46, 56-58, 61 and 133, as interpreted, are directed to a genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding polypeptides of any function or several distinct activities; i.e., any isolated polynucleotide having at least 95% nucleic acid sequence identity with polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions (as in claims 1 and 46), vector comprising said polynucleotide (as in claims 56-58), isolated host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133).

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there are no structural limitations or structure-function correlationship recited in claims with regard to the members of the genus of polynucleotides and encoded polypeptides claimed in claim 1, 46, 56-58, 61 and 133 i.e., any isolated polynucleotide having at least 95% nucleic acid sequence identity with

polynucleotide sequence of SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70 consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions (as in claims 1 and 46), vector comprising said polynucleotide (as in claims 56-58), isolated host cells comprising said polynucleotides (as in claim 61) and a micro-array comprising said polynucleotides (as in claim 133).

A sufficient written description of a genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides defined by their nucleotide sequence or a recitation of structure-function correlated features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, the genus of nucleic acids wherein said nucleic acids encompass a large number of variant polynucleotides encoding polypeptides of any function or several distinct activities. While the specification in the instant application discloses the structure of an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide of SEQ ID NO: 8 having glucoamylase activity, isolated host cells and micro-array comprising the polynucleotide and said polynucleotide (SEQ ID NO: 7) is not representative of the structure and function of all members of the claimed genus. The specification fails to disclose by any relevant, identifying characteristics or functional properties of all the members of the genus i.e., any information as to the structures associated with functions.

The genus of polynucleotides and encoding polypeptides required in the claimed invention is an extremely large structurally and functionally variable genus. While the

argument can be made that the recited genus of polynucleotides is adequately described by the disclosure of the structure of an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide with an amino acid sequence of SEQ ID NO: 8 having glucoamylase activity, since one could use structural homology to isolate those polynucleotide and encoding polypeptides recited in the claims. As taught by the art, even highly structurally homologous polynucleotides and encoded polypeptides do not necessarily share the same function. For example, Witkowski et al., (Biochemistry 38:11643-11650, 1999), teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β̃-ketoacyl synthase activity. Seffernick et al., (J. Bacteriol. 183(8): 2405-2410, 2001), teaches that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al., (Science 282:1315-1317, 1998), teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, the claimed genera of polynucleotides include encoding polypeptides having widely variable structure and associated functions, since minor changes in structure may result in changes affecting function and no additional information correlating structure with several distinct functions has been provided.

Due to the fact that the specification only discloses an isolated polynucleotide of SEQ ID NO: 7 encoding a polypeptide having an glucoamylase activity, isolated host

cells and a micro-array comprising the polynucleotide, and the lack of description of any additional species/variants/mutants/recombinants by any relevant, identifying characteristics or properties or structure-function correlationship for the cited several distinct functions/activities, one of skill in the art would not recognize from the disclosure that applicant was in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In support of their request that the prior rejection of claims 1, 46, 56-58, 61 and 133 under 35 U.S.C. 112, first paragraph, for insufficient written description be withdrawn applicants' provide the following argument that are very similar to the arguments provided for traversing the enablement rejection.

"The instant amendment to the claims and the reasons stated above address this issue…" (page 16 of applicants' response dated 04/21/09).

Reply: Applicants' arguments have been considered and are not found to be persuasive for the scientific reasons cited above in written-description rejection and examiner's reply provided above in maintaining the enablement rejection.

As argued above (see enablement rejection above), the broadest interpretation of claims encompasses a genus of mutant/variant polynucleotides of SEQ ID NO: 7 and encoding polypeptides with any structure with the associated function i.e., a polynucleotide sequence having 95% sequence identity to SEQ ID NO: 7 encoding a polypeptide having glucoamylase activity or a nucleic acid probe comprising at least 70

consecutive base of SEQ ID NO: 7, wherein said probe identifies said nucleic acid under any binding or hybridization conditions. The specification provides only a single species i.e., an isolated polynucleotide of SEQ ID NO: 7 encoding a full-length polypeptide of SEQ ID NO: 8 with glucoamylase activity of the recited genus, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the required genus. Examiner continues to hold the position that the genus of polynucleotides and encoded polypeptides with the associated function required in the claimed invention is an extremely large structurally variable genus, and thus claimed genus encompasses an essentially unlimited number of "undefined structural derivatives thereof" mutants, variants of said isolated polynucleotide having at least 95% nucleic acid sequence identity with an isolated polynucleotide of SEQ ID NO: 7 or said polynucleotide sequence encoding enzymatically active fragments thereof of SEQ ID NO: 8.

For these reasons, claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph for written-description.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1) claims 133 and 275 are objected for various informalities.

2) Claims 1, 46, 56-58, 61 and 133 are rejected under 35 U.S.C. 112, first paragraph for enablement and written description.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims,

Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652